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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09 762,842	04 30 2001	Akira Murasugi	SPO-112	1096

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EXAMINER

QIAN, CELINE X

ART UNIT PAPER NUMBER

2636

DATE MAILED: 02 14 2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/762,842

Applicant(s)

MURASUGI ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 6) ☐ Other: _____

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DETAILED ACTION

Claims 1-14 are pending in the application.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

The specification refers to 17 figures. However, no drawings have been submitted. Applicants should remove all references to the drawings from the specification.

Specification

The disclosure is objected to because of the following informalities: There is no page number throughout the specification.

Appropriate correction is required.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

There are several amino acid sequences in the specification lack sequence identifier. It is unclear whether they are included in the sequence listing. If not, a new paper copy and computer readable form is required.

Claim Rejections - 35 USC § 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 7, 9, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to the yeast transformant strain pIC9DP-hMK/SMD1168 and pPIC9-hPTN/GS115 and methods of using these strains to produce protein. Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112. Courts have recognized the necessity and desirability of permitting an applicant for a patent to supplement the written disclosure in an application with a deposit of biological material which is essential to meet some requirement of the statute with respect to the claimed invention. *Merck and Co., Inc. v. Chase Chemical Co.*, 273 F. Supp. 68, 155 USPQ 139 (D. N.J. 1967); *In re Argoudelis*, 434 F.2d 666, 168 USPQ 99 (CCPA 1970).

The yeast transformant strains claimed or used in the claimed method are not readily reproducible by the teaching of the specification because the copy number and integration site result from for each transformation process will be different, hence the genetic material of the yeast strain will be different. Therefore, Applicant must make a biological deposit of these two yeast transformant strains. The deposit rules (37 CFR 1.801 - 1.809) set forth examining

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procedures and conditions of deposit which must be satisfied when a deposit is required. See MPEP 2402-2404.

Complete information should include a declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following (see 37 CFR 1.801 through 1.809):

- 1) Identifies declarant.
- 2) States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.
- 3) States that the deposited material has been accorded a specific accession number.
- 4) States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.
- 5) States the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C. § 122.
- 6) States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty years after the date of deposit or for the enforceable life of the patent, whichever period longer.
- 7) That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and

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further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent. Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-14, the word "derived" renders the claims indefinite because the nature and number of derivative process are unknown. As such, the metes and bounds of the claims cannot be established.

Regarding claims 1-4 and 10, the term "5' AOX1 and 3' AXO1" renders the claims indefinite because the claimed subject matter is not clear. In other words, it is unclear whether

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Applicants are referring to sequences 5', 3' to the AOX1 protein or gene, 5', 3' sequences of the AOX1 protein or gene.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al (WO 92/13951), in view of Tomomura et al (1990, JBC, Vol. 265, No. 18, pp. 10765-10770) and Li et al (1990, Science, Vol.250, pp.1690-1694).

Davis et al. teach a yeast expression system based on methylotrophic yeast *Pichia pastoris* for production of human serum albumin. Davis et al. teach an expression vector comprising a promoter sequence of AOX1 gene, a signal sequence of $\alpha 1$ factor isolated from *Saccharomyces cerevisiae*, a nucleic acid sequence encoding human serum albumin, a transcription termination sequence from AOX1 gene, a selection marker gene, a replication origin functioning in *E.coli*.

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and a sequence homologous to 5' and 3' of the AOX1 gene for homologous recombination of the expression vector (see page 4, lines 11-16, page 7, 2nd paragraph, page 12, 2nd paragraph, page 14, lines 4-7 and 3rd paragraph, page 15, lines 5-11, page 18-19). Davis et al. further teach a yeast transformant comprising said vector and a method of producing human serum albumin polypeptide by culturing said yeast transformant (page 40-45, example 2 and 3). However, Davis et al. do not teach such a expression system for producing intact MK family proteins.

Tomomura et al. teach the nucleotide sequences and amino acid sequences encoding MK1, MK2 and MK3 (see page 10766, Figure 2).

Li et al. teach the cloning and expression of a MK family protein, PTN. Li et al. also teach the nucleotide and amino acid sequences encoding PTN protein.

Based on the combination teaching of Davis et al., Tomomura et al and Li et al., it would have been obvious to one of ordinary skill of art to produce MK family protein by using the methylotrophic yeast system taught by Davis et al. The ordinary artisan would have been motivated to do so because Davis et al. teach that this system would overcome the major problems associated with *S. cerevisiae* expression system such as loss of selection for plasmid maintenance and distribution (see page 4, lines 12-16). Since nucleotide sequences encoding MK1, MK2, MK3 and PTN have been taught by Tomomura et al. and Li et al., replacing the human albumin sequence with MK and PTN sequences is just routine experimentation to one of ordinary skill of art at the time of filing. Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation of success to make an expression vector for secretory expression of an intact MK family protein by methylotrophic yeast, a yeast transformant comprising said vector and producing MK protein by culturing said yeast transformant.

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Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time of filing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
February 7, 2003

Anne-Marie Falk
ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER